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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,427	03/13/2001	Peter Andersen	670001-2002.5	2084

7590 12/30/2002

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EXAMINER	
SWARTZ, RODNEY P	
ART UNIT	PAPER NUMBER
1645	13

DATE MAILED: 12/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/805,427	ANDERSEN ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23September2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *12-20,22,24 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,21,23 and 25-30* is/are rejected.

7)☒ Claim(s) *21,23 and 25* is/are objected to.

8)☒ Claim(s) *1-31* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' Response to Restriction Requirement, received 23September2002, paper#12, is acknowledged.

Applicants elect, with traverse, Invention I, claims 1-11, 21, 23, and 25, drawn to polypeptides and method of making, classified in class 424, subclass 248.1. The traversal is on the grounds that searching each of the inventions would likely be co-extensive because all relate to fragments of *M. tuberculosis*. This is not found persuasive because of the reasons put forth in the original Restriction Requirement.

The requirement is still deemed proper and is therefore made FINAL.

2. New claims 26-31 have been added. It is noted that the Response, page 2, line 20, requests the addition of only 26-30, but lists claims 26-31.

3. Clarification is required concerning what applicants request for the disposition of the remaining claims because of the uncertainty of the statement on page 5, paragraph 4, that "Should the Examiner make the restriction requirement final, claims 23 and 25 may be canceled along with the remaining claims of the non-elected groups, e.g., upon an indication of allowable subject manner."

4. The request for the deletion of an inventor in this nonprovisional application under 37 CFR 1.48(b) is deficient because:

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently

named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

5. Claims 1-31 are pending. Claims 12-20, 22, 24, and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Claim 31 is drawn to a method of vaccination using polypeptides and as such is included in nonelected Invention II.

6. Claims 1-11, 21, 23, and 25-30 are under consideration.

Drawings

7. This application has been filed with drawings which are acceptable for examination purposes only. The drawings are objected to for the reasons set forth on the attached form PTO-948.

Priority

8. The current status of the applications listed in the priority statement should be updated.

9. Acknowledgment is made of applicant's claim for foreign priority based on PA199701277 filed in Denmark on 11November1997. It is noted, however, that applicant has not filed a certified English translation of the application as delineated in 35 U.S.C. 119(b). Until a certified English translation of the application is submitted, the priority date is that of the provision application, 60/070,488.

In addition, the claim of priority of the Denmark application should be listed in the first paragraph of the specification.

Specification

10. The disclosure is objected to because of the following informalities:

a) page 1, as stated in the amendment of paper#12, line 7 of priority paragraph, "PCT/DK94/00273" should be "PCT/DK94/00270"; line 9 of priority paragraph, "which is claims priority" should be "which claims priority",

b) page 2, line 27 "organised programmes" should be "organized programs",

c) page 7, line 19, "characterised" should be "characterized",

d) page 12, line 7, "recognised" should be "recognized"; line 20, "analysing" should be "analyzing",

e) page 13, line 5, "recognised" should be "recognized",

f) page 19, line 24, "immunising" should be "immunizing"; line 29, "synthesising" should be "synthesizing",

Appropriate correction is required.

Claim Objections

11. Claims 23 and 25 are objected to because the claims are directed to nonelected inventions.

Claims 23 and 25 comprise embodiments which are directed to nucleic acid compositions.

12. Claims 21 and 25 are objected to because the claims refer to compositions according to nonelected claims.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claim 9 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101. See for example, *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475(D.D.C. 1966).

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 1-11, 21, 23, 25-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to polypeptides which comprise ≥70% sequence identity with a fusion polypeptide comprising ≥1 stretch of amino acids constituting a T-cell epitope derived from the *M. tuberculosis* protein ESAT-6 and a second amino acid sequence including ≥1 stretch of amino acids constituting a T-cell epitope derived from the *M. tuberculosis* protein Ag85B.

It is uncleared what are the metes and bounds of "derived". The claim is vague and indefinite in the use of the phrase "derivative" because it is unclear how the claimed product is undergoing any kind of chemical modification as implied by the recitation of "derivative". Therefore, there is no way for a person of skill in the art to ascribe a discrete and identifiable definition to said phrase.

Because there is no sequence listing for the fusion polypeptide, it is uncleared what are the metes and bounds for determining sequence identity for the analogues of the fusion polypeptide having ≥70% identity.

18. Claims 8, 9, 11, 25, and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a composition, for use as a vaccine, comprising a polypeptide comprising *M. tuberculosis* antigens ESAT-6 and Ag85B. Because there are no restriction on the type of hosts, the scope includes humans.

The specification teaches that the "Field of Invention" is drawn to new fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from *M. tuberculosis* and a tuberculosis subunit vaccine comprising at least one fusion protein. The discussion of the "General Background" is mostly directed to human tuberculosis and historically, the failure of effective vaccines to protect humans against infection with *M. tuberculosis* even though the vaccines were successful in animals. The discussion states that animal tuberculosis is caused by *M. bovis*. Therefore, it appears that the emphasis of the instant application is to provide a successful subunit vaccine for humans in combating/preventing infection with *M. tuberculosis*.

However, the only examples taught in the instant specification do not involve protection of humans against infection with *M. tuberculosis*, but only laboratory animals, i.e., guinea pigs, mice, and monkeys, which are not hosts for normal infection with *M. tuberculosis*.

The history of vaccination in humans against *Mycobacterial* disease is notorious for a lack of successful protection. In addition, at the time of filing of the instant specification, there remained a lack of correlation of success in animal models with successful vaccination of humans against mycobacterial disease, as evidenced by the review article, "Evaluation of the Protective Potency of New Tuberculosis Vaccines", *Review of Infectious Diseases*, Vol. 11, Supplement 2, pages S484-S490, March-April 1989.

Therefore, based upon the historical lack of any effective vaccinating agent, whole cell or subunit, other than BCG for protection of humans against *M. tuberculosis*, and the lack in the instant application of any human data showing the instantly claimed agent being effective for protection of humans against *M. tuberculosis*, the instant specification does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, i.e., a vaccinating agent for promoting, in humans, an effective immune response against *M. tuberculosis*.

19. Claims 8, 9, 11, 25, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a subunit vaccinating agent for experimentally infected nonhuman laboratory animals, does not reasonably provide enablement for a subunit vaccinating agent against *M. tuberculosis* for humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention is a composition, for use as a vaccine, comprising a polypeptide comprising *M. tuberculosis* antigens ESAT-6 and Ag85B. Because there are no restriction on the type of hosts, the scope includes humans.

The state of the prior art - there is a lack of predictability in the art for successful vaccines for humans against *M. tuberculosis* utilizing any agent other than whole viable cell *M. bovis* BCG. The history of vaccination in humans against *Mycobacterial* disease is notorious for a lack of successful protection. In addition, at the time of filing of the instant specification, there remained a lack of correlation of success in animal models with successful vaccination of humans against mycobacterial disease, as evidenced by the review article, "Evaluation of the Protective Potency of New Tuberculosis Vaccines", *Review of Infectious Diseases*, Vol. 11, Supplement 2, pages S484-S490, March-April 1989.

The amount of direction or guidance present - The specification teaches that the "Field of Invention" is drawn to new fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from *M. tuberculosis* and a tuberculosis subunit vaccine comprising at least one fusion protein. The discussion of the "General Background" is mostly directed to human tuberculosis and historically, the failure of effective vaccines to protect humans against infection with *M. tuberculosis* even though the vaccines were successful in animals. The discussion states that animal tuberculosis is caused by *M. bovis*. Therefore, it appears that the emphasis of the instant application is to provide a successful subunit vaccine for humans in combating/preventing infection with *M. tuberculosis*.

The presence or absence of working examples - the only examples taught in the instant specification do not involve protection of humans against infection with *M. tuberculosis*, but only experimentally infected laboratory animals, i.e., guinea pigs, mice, and monkeys, which are not hosts for normal infection with *M. tuberculosis*.

The relative skill of those in the art for production of vaccines against *M. tuberculosis* in experimentally infected animals is high and has been successful. However, to date, other than *M. bovis* BCG, the production of any other vaccine against *M. tuberculosis* in humans has been totally unsuccessful.

The breadth of the claims encompasses not only animals experimentally infected with *M. tuberculosis*, but also humans exposed to or already infected with *M. tuberculosis*.

The quantity of experimentation necessary to produce a vaccinating agent in humans to protect against *M. tuberculosis* infection constitutes at this point in time merely an invitation for experimentation without a reasonable expectation of success.

20. Claims 8, 9, 11, 25, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccinating agent constructed from *M. tuberculosis* proteins for nonhuman laboratory animals against *M. tuberculosis* infection, does not reasonably provide enablement for a vaccinating agent constructed from *M. tuberculosis* proteins which cross-protects against any/all other species of the genus *Mycobacterium*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The nature of the invention is a composition, for use as a vaccine, comprising a polypeptide comprising *M. tuberculosis* antigens ESAT-6 and Ag85B. The vaccine can be used either prophylactically or therapeutically in subjects already infected with any virulent mycobacterium.

The presence or absence of working examples - the only examples taught in the instant specification involve protection of experimentally infected laboratory animals against infection with *M. tuberculosis.* The instant specification does not indicate any cross-protection using the instantly claimed fusion protein.

Conclusion

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., whose telephone number is (703) 308-4244. The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (703)308-3909. The facsimile telephone number for the Art Unit Group is (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

Art Unit 1645
December 27, 2002

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER